

TITLE: Preparation of novel 4-(1,2,3,4-tetrahydroisoquinolin-2-yl)pyrimidines possessing an excellent anti-secretory activity

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PATENT ASSIGNEE(S): Yuhan Corp., S. Korea

SOURCE: PCT Int. Appl., 110 pp.  
CODEN: PIXXD2

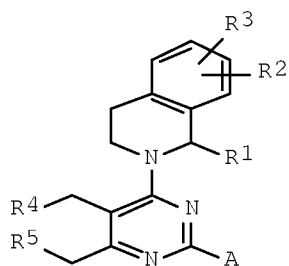
DOCUMENT TYPE: Patent

LANGUAGE: English

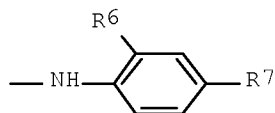
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.  | KIND              | DATE     | APPLICATION NO.  | DATE           |
|---|-------------------|----------|------------------|----------------|
| WO 9843968  | A1                | 19981008 | WO 1998-KR58     | 19980324 <--   |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW |                   |          |                  |                |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG  |                   |          |                  |                |
| IN 188411   | A1                | 20020921 | IN 1998-DE724    | 19980323 <--   |
| CA 2284795  | A1                | 19981008 | CA 1998-2284795  | 19980324 <--   |
| CA 2284795  | C                 | 20040120 |                  |                |
| AU 9865239  | A                 | 19981022 | AU 1998-65239    | 19980324 <--   |
| AU 720385   | B2                | 20000601 |                  |                |
| BR 9808070  | A                 | 20000308 | BR 1998-8070     | 19980324 <--   |
| TR 9902383  | T2                | 20000621 | TR 1999-2383     | 19980324 <--   |
| EP 1015444  | A1                | 20000705 | EP 1998-911242   | 19980324 <--   |
| EP 1015444  | B1                | 20030528 |                  |                |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI   |                   |          |                  |                |
| JP 2000513014   | T                 | 20001003 | JP 1998-541487   | 19980324 <--   |
| JP 3176379  | B2                | 20010618 |                  |                |
| HU 2000000851   | A2                | 20010428 | HU 2000-851      | 19980324 <--   |
| HU 2000000851   | A3                | 20020429 |                  |                |
| RU 2203894  | C2                | 20030510 | RU 1999-122603   | 19980324 <--   |
| AT 241613   | T                 | 20030615 | AT 1998-911242   | 19980324 <--   |
| CN 1118464  | B                 | 20030820 | CN 1998-803765   | 19980324 <--   |
| PT 1015444  | T                 | 20031031 | PT 1998-911242   | 19980324 <--   |
| ES 2200324  | T3                | 20040301 | ES 1998-911242   | 19980324 <--   |
| TW 542831   | B                 | 20030721 | TW 1998-87104605 | 19980327 <--   |
| MX 9908822  | A                 | 20000731 | MX 1999-8822     | 19990924 <--   |
| US 6352993  | B1                | 20020305 | US 1999-381814   | 19990924 <--   |
| HK 1026418  | A1                | 20040305 | HK 2000-105563   | 20000905 <--   |
| PRIORITY APPLN. INFO.:  |                   |          | KR 1997-10862    | A 19970327 <-- |
|   |                   |          | KR 1997-10863    | A 19970327 <-- |
|   |                   |          | WO 1998-KR58     | W 19980324 <-- |
| OTHER SOURCE(S):  | MARPAT 129:302651 |          |                  |                |
| GI  |                   |          |                  |                |



I



II

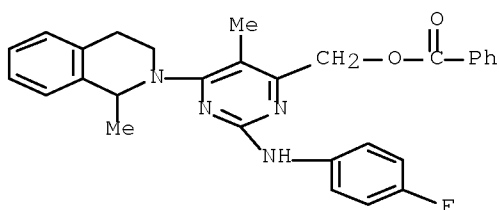
AB The title compds. [I; when A = piperidin-1-yl, NHB (wherein B = C3-4 alkyl, C3-4 alkenyl, C3-7 cycloalkyl, etc.); R1 = H, Me; R2-R5 = H; and A = II when R1 = HOCH2, C1-3 alkoxyethyl; R2-R6 = H, and R7 = H, halo; or when R1 = H, Me; R7 = H, halo; and one or two of R2-R6 = OH, MeO, CC(O)Z (wherein Z = C1-4 alkyl, C2-4 alkenyl, cycloalkyl, etc.)], useful in the treatment of peptic ulcers, were prepared. Thus, reaction of allylamine with 2-chloro-5,6-dimethyl-4-(1,2,3,4-tetrahydroisoquinolin-2-yl)pyrimidine in the presence of Et3N in DMF afforded 28.5% I.HCl [A = H2C:CHCH2NH; R1-R5 = H] which showed IC50 of 7.85  $\mu$ M against H+/K+-ATPase.

IT 214538-62-2P 214538-66-6P 214538-70-2P  
214538-73-5P 214538-77-9P 214538-79-1P  
214538-81-5P 214538-83-7P 214538-89-3P  
214538-91-7P 214538-94-0P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of novel 4-(1,2,3,4-tetrahydroisoquinolin-2-yl)pyrimidines possessing an excellent anti-secretory activity)

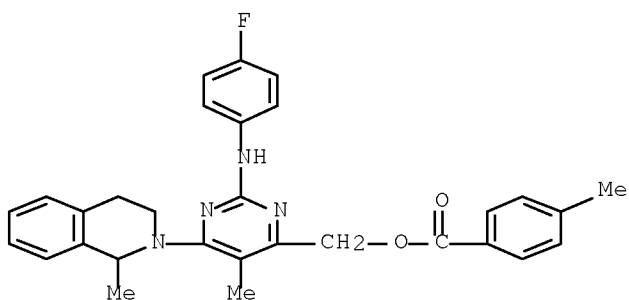
RN 214538-62-2 ZCAPLUS

CN 4-Pyrimidinemethanol, 6-(3,4-dihydro-1-methyl-2(1H)-isoquinolinyl)-2-[(4-fluorophenyl)amino]-5-methyl-, benzoate (ester) (9CI) (CA INDEX NAME)



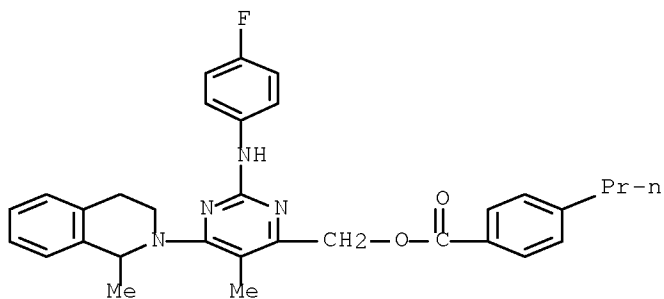
RN 214538-66-6 ZCAPLUS

CN Benzoic acid, 4-methyl-, [6-(3,4-dihydro-1-methyl-2(1H)-isoquinolinyl)-2-[(4-fluorophenyl)amino]-5-methyl-4-pyrimidinyl]methyl ester (CA INDEX NAME)



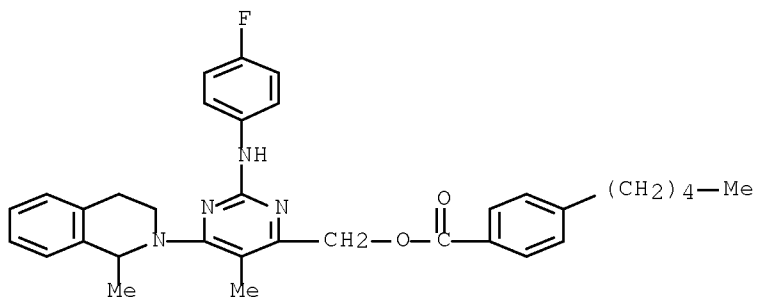
RN 214538-70-2 ZCAPLUS

CN Benzoic acid, 4-propyl-, [6-(3,4-dihydro-1-methyl-2(1H)-isoquinolinyl)-2-[(4-fluorophenyl)amino]-5-methyl-4-pyrimidinyl]methyl ester (CA INDEX NAME)



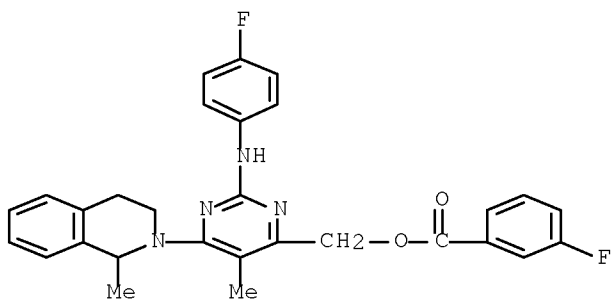
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CN Benzoic acid, 4-pentyl-, [6-(3,4-dihydro-1-methyl-2(1H)-isoquinolinyl)-2-[(4-fluorophenyl)amino]-5-methyl-4-pyrimidinyl]methyl ester (CA INDEX NAME)



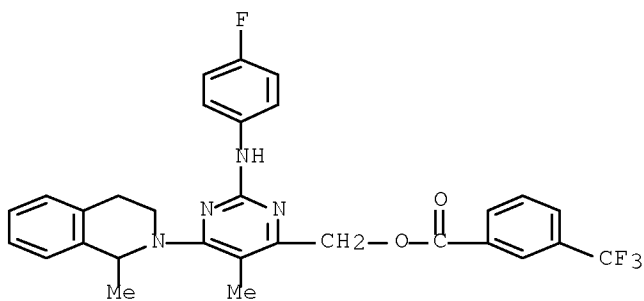
RN 214538-77-9 ZCAPLUS

CN Benzoic acid, 3-fluoro-, [6-(3,4-dihydro-1-methyl-2(1H)-isoquinolinyl)-2-[(4-fluorophenyl)amino]-5-methyl-4-pyrimidinyl]methyl ester (CA INDEX NAME)



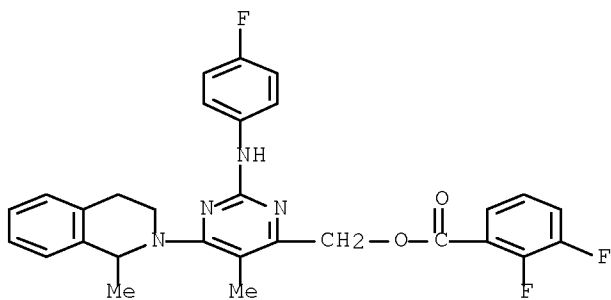
RN 214538-79-1 ZCAPLUS

CN Benzoic acid, 3-(trifluoromethyl)-, [6-(3,4-dihydro-1-methyl-2(1H)-isoquinolinyl)-2-[(4-fluorophenyl)amino]-5-methyl-4-pyrimidinyl]methyl ester (CA INDEX NAME)



RN 214538-81-5 ZCAPLUS

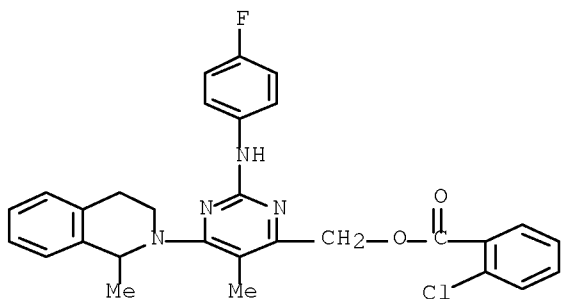
CN Benzoic acid, 2,3-difluoro-, [6-(3,4-dihydro-1-methyl-2(1H)-isoquinolinyl)-2-[(4-fluorophenyl)amino]-5-methyl-4-pyrimidinyl]methyl ester (CA INDEX NAME)



RN 214538-83-7 ZCAPLUS

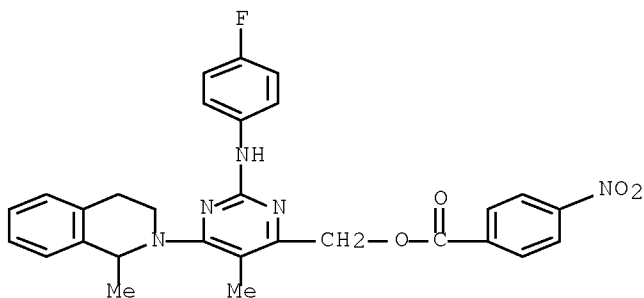
CN Benzoic acid, 2-chloro-, [6-(3,4-dihydro-1-methyl-2(1H)-isoquinolinyl)-2-

[(4-fluorophenyl)amino]-5-methyl-4-pyrimidinyl)methyl ester (CA INDEX NAME)



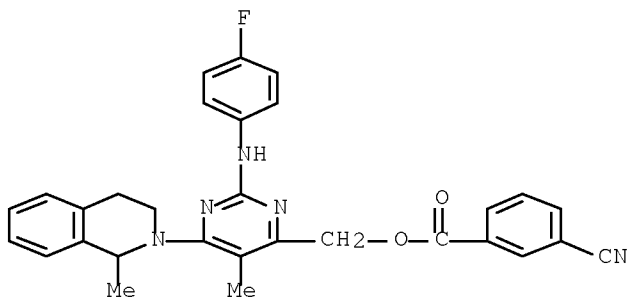
RN 214538-89-3 ZCAPLUS

CN 4-Pyrimidinemethanol, 6-(3,4-dihydro-1-methyl-2(1H)-isoquinolinyl)-2-[(4-fluorophenyl)amino]-5-methyl-, 4-nitrobenzoate (ester) (9CI) (CA INDEX NAME)



RN 214538-91-7 ZCAPLUS

CN Benzoic acid, 3-cyano-, [6-(3,4-dihydro-1-methyl-2(1H)-isoquinolinyl)-2-[(4-fluorophenyl)amino]-5-methyl-4-pyrimidinyl)methyl ester (CA INDEX NAME)



RN 214538-94-0 ZCAPLUS

CN 1-Naphthalenecarboxylic acid, [6-(3,4-dihydro-1-methyl-2(1H)-  
isoquinolinyl)-2-[(4-fluorophenyl)amino]-5-methyl-4-pyrimidinyl]methyl  
ester (CA INDEX NAME)

